DETAILED ACTION

ACKNOWLEDGMENT OF PRIORITY, IDS, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

1. This application filed under 35 U.S.C. 371 on 07/18/05 having a filing date of 03/07/03 of PCT/EPO03/02356. Acknowledgement is made of Applicant's claim priority based on German Application Number 102 11 555.9 having filing date of 03/15/02. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file.

The information disclosure statement (IDS) and Form PTO-1449 filed 10/24/05 and the response to the restriction requirement filed 01/22/08, respectively are acknowledged, entered and considered. The references cited in the Search Report from the EPO have been considered, but will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO/SB/08A and 08B form, must be filed within the set period for reply to this Office action. Claims 1-42 are now pending in the application.

OBJECTION TO THE SPECIFICATION

2. The specification is objected because there are no Headings disclosed in the disclosure and the following guidelines illustrate the preferred layout and content for patent application. These guidelines are suggested for the Applicant's use:

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.

(b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) Or

REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)

(e) BACKGROUND OF THE INVENTION.

(1) Field of the Invention.

(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) BRIEF SUMMARY OF THE INVENTION.

(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(h) DETAILED DESCRIPTION OF THE INVENTION.

(i) CLAIM OR CLAIMS (commencing on a separate sheet).

(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

3. Also, the specification is objected because the priority data of this application should be updated in the specification. Appropriate correction is required.

4. Further, the inclusion of Figures in Example 1 is objected because the Figures should be presented after the claims on separate pages and accompanied by a Brief Description. Also, Figure 3 is objected in the recitation "Konzentration". It should be amended to recite "Concentration". The text refers to Fig 2 at page 6 as demonstrating concentration response, but it is Fig 3 which does. Thus, appropriate correction is required.

OBJECTION OF THE TITLE

5. The title of the invention is objected to because of its excessive length, as shown by the fact that the complete title proposed by Applicant can not be fitted on the Official filing receipt or on the patent application. Correction is required. See 37 CFR 1.72(a) and MPEP § 606.

ELECTION WITHOUT TRAVERSE

6. Applicant's election of Group II (claims 6-15 and 26-31), (Lys[Z(NO_2)]-thiazolidide as the species of DP IV inhibitor and benign follicular hyperproliferation conditions as the species of condition to be treated in the reply filed 01/22/08 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without** traverse (MPEP § 818.03(a)). Claims 6-8, 10-13 and 15 and 26-27, 29-30 will be examined insofar as they read on (Lys[Z(NO_2)]-thiazolidide (N^{ε}-4-nitrobenzyloxycarbonyl-L—Lysine thiazolidide) as the species of DP IV inhibitor and benign follicular hyperproliferation conditions as the species of condition to be treated. Claims 9, 14, 28 and 31 are withdrawn from consideration as being drawn to a nonelected species, there being no allowable generic claim. The claims now broadly encompass non-elected subject matter.

OBJECTION OF THE CLAIMS

7. Claims 6-15 and 26-31 are objected of numerous misspellings. Examples are "inhabitation" in claim 6 and "tryptophane" in claim 7. Further, the claims would benefit greatly from grammatical revisions and through use of standard U.S. claim formats.

CLAIMS REJECTION-35 U.S.C. 112, 1st PARAGRAPH

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8, 10-13 and 15 and 26-27, and 29-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of DNA synthesis of human cell line SZ95, does not reasonably provide enablement for the inhibition of proliferation of any sebaceous cells or treat all of these diseases as claimed in claims 6-8, 10-13 and 15 and 26-27, 29-30. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the instant case, the elected claims are drawn to a method for inhibition of the proliferation (DNA system) of human sebaceous cells comprising utilizing inhibitors of dipeptidylpeptidase IV (DP IV) wherein the DP IV inhibitor is (Lys-[ZNO_2])-thiazolidide and/or inhibitors of alanyl aminopeptidase (aminopeptidase N or APN) and of enzymes having similar substrate specificity (APN-analogous enzyme activity) for the inhibition of proliferation (DNA synthesis) of human sebaceous cells and in treating the conditions of benign follicular hyperproliferation by singular or repeated administration of pharmaceutical preparations to a patient with corresponding disease pattern recited in claims 15 and 26-27 and 29-30 by using the claimed compounds in the manner claimed in claims 6-8, 10-13 and 15 and 26-27, 29-30.

The instant specification provides very little guidance in regard to making/using the elected species of DP IV inhibitor for treating the conditions elected. Example 1 and Figures 1-3 disclose the inhibition of DNA synthesis of human cell line SZ95, an immortalized sebocyte alleged to be an art accepted model of acne, by the incubation with synthetic inhibitor DP IV

and/or APN *in vitro*. Further, there is only utilization of the compound claimed but there is no disclosure of method for administration nor amount or dosages to be administered or a specific target of population. Thus, there is no enablement in the instant specification for a method for inhibition of the proliferation (DNA synthesis) of human sebaceous cells and in treating the condition of benign follicular hyperproliferation by singular or repeated administration of pharmaceutical preparations to a patient with corresponding disease patterns as claimed. The instant specification on page 3, last paragraph alleges that the use of DP IV and/or APN inhibitors would represent a completely new, presumably very effective, possibly cost effective therapy form and a valuable alternative component of existing therapy concepts of the above-referenced diseases. However, there is no pharmaceutical formulation administered to a patient an effective amount of the claimed compounds to **inhibit the proliferation of human sebaceous cells and/or to treat disease conditions of benign follicular hyperproliferation in a patient,** and as such, does not sufficiently provide ample enablement as claimed in the instant invention.

There is no *in vivo* showing or data or a single example to demonstrate the administration of an effective amount of DP IV and/or APN inhibitors for the effectiveness of the method for inhibition of the proliferation of human sebaceous cells by administering a pharmaceutical preparation to a patient with corresponding disease pattern in the manner claimed.

9. Claims 6-8, 10-13 and 15 and 26-27, and 29-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are no teachings in the specification to show the enablement of a method for **inhibition** of the proliferation of human sebaceous cells, in acne, including the singular or the repeated administration of a pharmaceutical preparation of the claimed compound to a patient with corresponding disease pattern, wherein the disease pattern and/or conditions are (acne, acneform follicular reactions, steatocystoma multiplex, naevi of sebaceous glands, senile sebaceous gland hypertrophy, seborrhea of the skin and of the hair), SAHA syndrome [seborrhea, acne, hirsutism, alopecia] and malign follicular hyperproliferation conditions(mixed tumors, sebaceomes, naevus sebaceous with malign development, sebaceous gland tumors, sebaceous gland CA) for **prevention** and **therapy of benign follicular hyperproliferation conditions**.

The specification discloses the various dermatological diseases and/or conditions which are associated with hyperproliferation and modified states of differentiation of sebocytes as recited above. The claims recite only utilizing the compounds claimed rather than administering the claimed compound to a specific population. Thus, there is no specific data or evidence or **even one example** to show a method for demonstrating the administration of an effective amount of DP IV and/or APN inhibitors for the effectiveness of the method for inhibition of the proliferation of human sebaceous cells by administering a pharmaceutical preparation to a patient with corresponding disease patterns in the manner claimed. Thus, the scope of **inhibition and treatment and/or prevention in a patient** in the manner claimed are not enabled and speculative.

Therefore, the administration of the formulation claimed to **treat and/or prevent all kinds of dermatological conditions and/or diseases in a patient**, which may include human or non-human, would include those preparation/formulation that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine under what condition, the claimed invention preparation/formulation is enabled, since a wide range of steps, processes and ingredients are contemplated and are encompassed as well as a method of **treating and/or preventing all kinds of dermatological conditions and/or diseases in a patient** (any patient). The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed.

Therefore, without guidance through working example(s), one of ordinary skill in the art would not predict from pages 1-4, Example 1 and Figures 1-3 of the instant specification to use a method for demonstrating the administration of an effective amount of DP IV and/or APN inhibitors for the effectiveness of the method for inhibition of the proliferation of human sebaceous cells by administering a pharmaceutical preparation to a patient with corresponding disease patterns in the manner claimed. Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CLAIMS REJECTION-35 U.S.C. § 102(e)

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6-8, 10-13 and 15 and 26-27, and 29-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Ansorge et al (U.S. Patent No. 7,229,969; this is a 371 of WO 02053170 filed 21 Dec 2001).

The elected claims are drawn to a method for inhibition of the proliferation (DNA system) of human sebaceous cells comprising utilizing inhibitors of dipeptidylpeptidase IV (DP IV) wherein the DP inhibitor is (Lys-[ZNO_2])-thiazolidide and/or inhibitors of alanyl aminopeptidase (aminopeptidase N or APN) and of enzymes having similar substrate specificity (APN-analogous enzyme activity) for the inhibition of proliferation (DNA synthesis) of human sebaceous cells and in treating the conditions of benign follicular hyperproliferation by singular or repeated administration of pharmaceutical preparations to a patient with corresponding disease pattern recited in claims 15 and 26-31 by using the claimed compounds in the manner claimed in claims 6-15 and 26-31.

The reference of Ansorge et al ('969 patent) discloses combination of inhibitors of DP IV such as (Lys-[ZNO_2])-thiazolidide having the same substrate specificity (DP IV-analogous enzymatic activity) and inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) and of

enzymes having the same substrate specificity (APN-analogous enzymatic activity) for inhibition and for treatment of diseases such as dermatological diseases with follicular and epidermal hyperkeratoses and enhanced proliferation of keratinocytes. Further, Figure 2 of the instant invention is identical with Figure 13 of '969 patent. Thus, sufficient evidence of similarity is deemed to be present between the instantly claimed invention of claims 6-15 and 26-31 and the '969 patent's teachings as disclosed in the abstract, col. 7, lines 43-45, Examples 1-13 and figure 13.

Therefore, in the absence of evidence to the contrary or specific structural limitations, the prior art teachings clearly discloses the use of the claimed compounds to inhibit the proliferation of human sebaceous cells and/or to treat dermatological disease conditions of benign follicular hyperproliferation in a patient, and as such anticipates claims 6-15 and 26-31 as drafted.

CITATION OF RELEVANT PRIOR ART

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ansorge et al (US 2005/0014699) disclose combinations of enzymes such as inhibitors alanyl aminopeptidase and dipeptidyl peptidase containing preparations and the use thereof.

CONCLUSION AND FUTURE CORRESPONDNCE

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABDEL A. MOHAMED whose telephone number is (571)272-0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mohamed/A. A. M./
Examiner, Art Unit 1654